

ORIGINAL ARTICLE

Acute *Campylobacter* spp. gastroenteritis in the Pediatric Emergency Department of a level II hospital

Gastroenterite aguda por *Campylobacter* spp. no Serviço de Urgência Pediátrica de um hospital de nível II

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ABSTRACT

Introduction: *Campylobacter* spp. is the main cause of pediatric acute bacterial gastroenteritis (ABG) in the European Union, with greater incidence in children under five years old. Most patients present complete recovery within days of infection, with no associated comorbidities. Antibiotic therapy should be reserved for severe cases.

Objectives: The aim of this study was to investigate the epidemiology, symptoms, treatment, and complications of *Campylobacter* spp. infection in pediatric patients with ABG.

Material and methods: Case-by-case review of the clinical records of patients evaluated in the Pediatric Emergency Department of a level II hospital with a diagnosis of ABG and *Campylobacter* spp. isolated from stool samples over a five-year period (2013-2017).

Results: Of the 1990 stool tests performed, 637 (32%) were positive for the presence of bacteria. *Campylobacter* spp. was identified in the samples of 459 patients (72%). Eighteen patients were excluded for insufficient data, making up a final sample of 441 patients, with a mean age of three years old. Clinically, patients presented with aqueous diarrhea (59.6%), bloody diarrhea (43.8%), bloody and mucus diarrhea (15.4%), mucus diarrhea (3.9%), vomiting (36.3%), abdominal pain (24.3%), fever (63%), seizures (0.9%), and rash (0.2%). Eighty-nine patients were hospitalized. Eleven patients received antibiotic therapy.

Discussion: This study represents the largest national case-by-case review of ABG by *Campylobacter* spp. in the pediatric population. *Campylobacter* was the main bacteria identified, mostly associated with self-limited disease.

Conclusion: A judicious use of stool tests allows etiological identification in ABG. The growing number of cases of ABG by *Campylobacter* spp. reinforces the need for better hygiene procedures.

Keywords: *Campylobacter*; child; gastroenteritis; hygiene

RESUMO

Introdução: *Campylobacter* spp. é a causa principal de gastroenterite aguda bacteriana (GAB) pediátrica na União Europeia, com maior incidência em crianças com idade inferior a cinco anos. A maioria dos doentes tem uma recuperação completa num período de dias da data de infeção, sem comorbilidades associadas. A antibioterapia deve ser reservada para casos mais graves.

Objetivo: O objetivo deste estudo foi avaliar a epidemiologia, sintomas, tratamento e complicações associadas à infeção por *Campylobacter* spp. em doentes pediátricos com GAB.

Material e métodos: Revisão dos casos clínicos de doentes avaliados no Serviço de Urgência Pediátrica de um hospital de nível II por um

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período de cinco anos (2013-2017) com diagnóstico de GAB e isolamento de *Campylobacter* spp. nas fezes.

Resultados: Dos 1990 testes coprológicos efetuados, 637 (32%) foram positivos para a presença de bactérias. *Campylobacter* spp. foi identificada em 459 doentes (72%). Dezoito doentes foram excluídos por falta de informação, constituindo uma amostra final de 441 doentes, com uma idade média de três anos. Clinicamente, os doentes apresentavam diarreia aquosa (59,6%), diarreia sanguinolenta (43,8%), diarreia mucosanguinolenta (15,4%), diarreia mucosa (3,9%), vômitos (36,3%), dor abdominal (24,3%), febre (63%), convulsões (0,9%) e exantema cutâneo (0,2%). Oitenta e nove doentes foram internados. Onze doentes receberam antibioterapia.

Discussão: Este estudo representa a maior revisão nacional até à data de casos de GAB por *Campylobacter* spp. na população pediátrica. *Campylobacter* foi a principal bactéria identificada, maioritariamente associada a doença autolimitada.

Conclusão: O uso racional de testes coprológicos permite a identificação etiológica na GAB. O aumento dos casos de GAB por *Campylobacter* spp. reforça a necessidade de melhor cuidados de higiene.

Palavras-chave: *Campylobacter*; criança; gastroenterite; higiene

INTRODUCTION

Infection by *Campylobacter* spp., in particular *C. jejuni* and *C. coli*, is the main cause of acute bacterial gastroenteritis (ABG) in Europe,¹ with a higher prevalence than reported for infections caused by *Salmonella* spp., *Shigella* spp., and enteropathogenic *Escherichia coli*.^{2,3} According to the latest report of the European Centre for Disease Prevention and Control, campylobacteriosis is the most frequently notified zoonotic disease in humans, with a growing incidence in recent years and the largest number of cases occurring in male children under five years old.⁴ In Portugal, recent data also shows an increasing prevalence of the disease, with *C. jejuni* being the most frequently identified etiological agent. Human campylobacteriosis is a compulsory notifiable disease since 2014.⁵

It is generally believed that *Campylobacter* acts by direct invasion of the intestinal epithelial cells, inducing an inflammatory process and producing a toxin.^{1,6,7} *C. jejuni* infection in humans is usually sporadic and more frequent during the Summer months. Most etiological agents come from animal reservoirs (birds, cattle, goats, and sheep) and are transmitted by ingestion of poorly cooked meat (mainly poultry), unpasteurized milk and milk derivatives, and untreated water, with human-to-human transmission being very rare.^{8,9}

C. jejuni causes aqueous diarrhea or diarrhea with mucus and/or blood in about half of cases. Other relatively frequent symptoms include fever, abdominal pain, nausea or vomiting, headache, and myalgia. The disease usually occurs 24-72 hours after ingestion of contaminated food or water and has an average duration of seven to ten days, although recurrences are not rare (25% of cases).^{9,10}

The diagnosis is usually established by isolation of the bacteria in stools and identification of the etiological organism through mass spectrometry or biochemical and molecular methods. It can also be accomplished by direct microscopy/dark-field microscopy, specific antigen detection, identification of the bacterium DNA through

polymerase chain reaction, and serology through ELISA technique.^{1,7,8}

Treatment consists of restoration of the fluid and electrolyte balance. Antimicrobial therapy is only recommended in cases of high risk of severe disease, namely presence of dysentery, high fever, extraintestinal disease, symptom worsening or recurrence, symptoms lasting more than one week, concomitant chronic conditions, immunodeficiency, or pregnancy, and in outbreak situations. Macrolides are the first-line treatment.^{1,10}

Campylobacteriosis is a self-limiting disease in most cases, particularly in healthy children, although complications have been reported, such as reactive arthritis, sepsis, Guillain-Barré syndrome, and hemolytic anemia.^{2,5}

The aims of this study were to estimate the prevalence of *Campylobacter* spp. in the stools of pediatric patients with ABG, and characterize cases regarding clinical and epidemiological features, therapeutic approach, and associated complications.

MATERIAL AND METHODS

A case-by-case review of the clinical records of patients evaluated in the Pediatric Emergency Department (ED) of a level II hospital between January 2013 and December 2017 was conducted. All patients with diagnosis of ABG by *Campylobacter* spp. were included. The diagnosis was established using a selective medium for isolation of *Campylobacter* spp. from stool samples and subsequent identification from a gallery of biochemical tests (API Campy).

Although the criteria for performing stool tests have some degree of individual variability, in the study hospital they are indicated in cases where the following signs/symptoms are present: frequent/intense abdominal cramps, high fever, prolonged diarrhea or diarrhea with mucus and/or blood, concomitant chronic conditions, immunodeficiency, and admission to the Pediatric Department with a diagnosis of ABG.

The following patient data were retrieved for clinical records: age, gender, date of Pediatric ED evaluation, area of residence, history of recent food intake, epidemiological context, clinical features (stool characteristics, presence of other symptoms), treatment, reason for admission, and disease progression.

Data were analyzed using the Statistical Package for the Social Sciences Program[®] (SPSS Inc., Chicago, IL) version 23, through measures of central tendency and dispersion for quantitative variables and absolute and relative frequencies for qualitative variables.

RESULTS

During the study period, 1990 stool tests were carried out in the Pediatric ED, 637 (32%) of which were positive for the presence of bacteria. *Campylobacter* spp. was identified in 459 cases (72%), followed by *Salmonella* spp. in 144 (22.6%), *Yersinia enterocolitica* in 37 (5.8%), and *Shigella* spp. in only one case (0.2%). No cases of *Aeromonas* spp. or *Escherichia coli* 0157 were detected. Bacterial coinfection was identified in four cases, one by *Campylobacter* spp. and *Yersinia enterocolitica*, one by *Yersinia enterocolitica* and *Shigella* spp., one by *Campylobacter* spp., *Yersinia enterocolitica*, and *Salmonella*, and one by *Campylobacter* spp. and *Salmonella*.

In addition to stool tests, virological stool examination was performed in 90.7% of patients with *Campylobacter* spp. isolated in stools, being positive in 7%: 4.1% for rotavirus, 0.7% for adenovirus, and 1.8% for both viruses.

From the 459 *Campylobacter*-positive stool tests, 18 were excluded for lack of data, making up a final sample of 441 patients, with a mean age of 3.2 years (standard deviation \pm 4.2; range 1 month–17

years) and male predominance (57.8%).

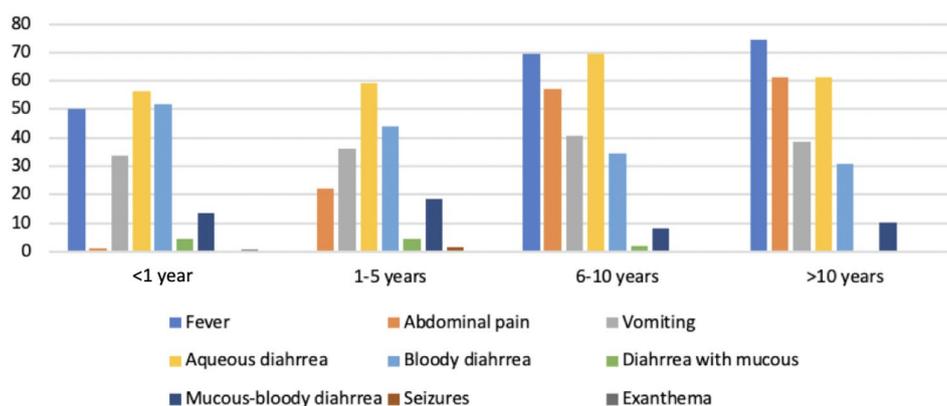
The infection was predominant in the months of Spring to Autumn, with 11.1% of cases occurring in May, 10.9% in August, and 10% in October. *C. jejuni* was the main species identified (372 cases; 85.3%), followed by *C. coli* (21 cases; 4.8%), and *C. upsaliensis* (2 cases; 0.5%). No newborn was admitted to the Pediatric ED with ABG due to *Campylobacter* spp. infection.

Children included in the study were stratified by age group into infants (<1 year old), one-to-five-year-olds, six-to-10-year-olds, and older than 10 years old. The highest incidence of infection was observed in children aged one to five years (n=243, 55.1%), followed by infants (n=110, 24.9%) and children aged six to 10 years (n=49, 11.1%), and the lowest incidence was seen in children older than 10 years (n=39, 8.8%). Differences in incidence rates were statistically significant (p=0.042). Infants were further stratified according to age group into one-to-three-month-olds and four-to-twelve-month-olds, with the highest incidence reported in the latter (n=86, 78.2%).

Most patients had no data about consumption of suspicious food (n=367, 83.2%), and 39 denied its intake (8.8%). In cases with identification of a possible bacteria food source, untreated water was the most frequent (3.6%). Epidemiological causes were identified in 12.7% of cases, through reports of concomitant cases of diarrhea in the family, with no data available for 55.1% of cases.

The forms of presentation included aqueous diarrhea (n=263, 59.6%), bloody diarrhea (n=193, 43.8%), mucous-bloody diarrhea (n=68, 15.4%), diarrhea with mucous (n=17, 3.9%), vomiting (n=160, 36.3%), abdominal pain (n=107, 24.3%), fever (n=278, 63.0%), seizures (n=4, 0.9%; all in the context of fever), and exanthema (n=1, 0.2%). Clinical presentation according to age group is depicted in

Figure 1.



ABG, acute bacterial gastroenteritis

Figure 1 - Clinical presentation of patients with ABG, according to age group

No statistically significant differences were found in clinical presentation across age groups, except for seizures, which mostly occurred in feverish context in children between one and five years old.

Among children observed in the Pediatric ED, 108 required a short hospital stay, and 104 were admitted to the Pediatric Department (PD; **Figure 2**). Admissions occurred mostly among infants younger than three months.

A total of 125 children (28.3%) were readmitted to the Pediatric ED for persistence or worsening of symptoms, 27 of whom (21.6%) were hospitalized (**Figure 3**).

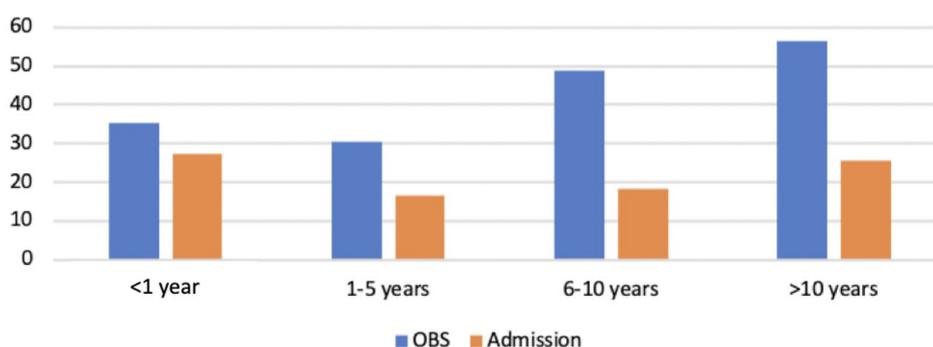
Of all patients admitted to the PD, 28.8% (n=30) were younger than 12 months. The average duration of hospital stay was 3.2 days (range 1–10 days). During hospital stay, 94.4% received some form of treatment, including intravenous fluids in 92% (n=82) and antibiotic

therapy in 12.4% (n=11; azithromycin in nine and clarithromycin in two). Four patients received antibiotic therapy directed at other coinfections.

A total of 143 samples were randomly selected for the study of antibiotic resistance patterns in the reference laboratory, with results showing resistance to quinolones in 93.7%, to tetracyclines in 83.2%, to macrolides in 11.9%, and to aminoglycosides in 0.7%.

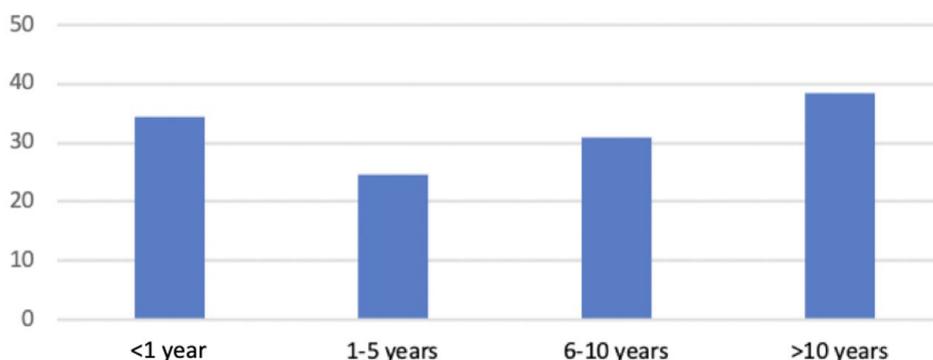
A total of 156 children (37.9%) developed complications, mostly dehydration (n=120, 67.4%), but also food refusal (n=44, 24.7%; **Figure 4**).

After hospital discharge, 280 children (63.5%) were reevaluated in outpatient setting. Control stool tests were carried out in 43.5%, with negative stool test results in 85.6% of these cases. A total of 15 children (3.4%) had more than one episode of ABG by *Campylobacter* spp. in the considered study period.



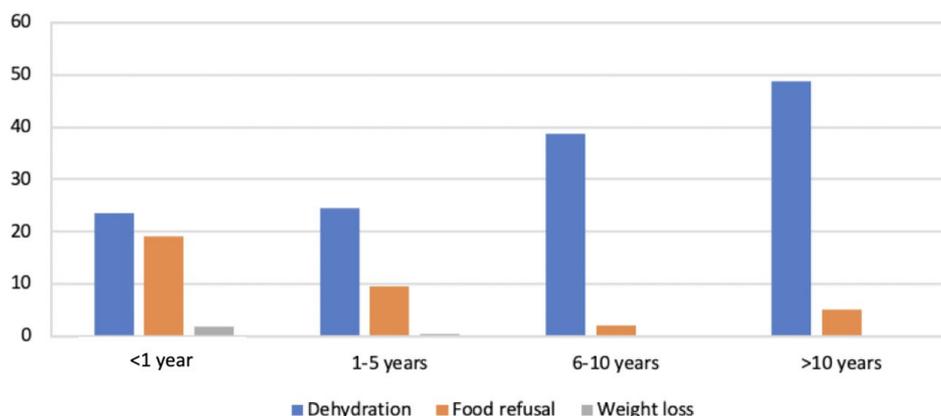
ABG, acute bacterial gastroenteritis; ED, Emergency Department; OBS, observation

Figure 2 - Destination of patients with ABG after observation in the ED, according to age group



ABG, acute bacterial gastroenteritis; ED, Emergency Department

Figure 3 - Readmission of patients with ABG to the ED, according to age group



ABG, acute bacterial gastroenteritis

Figure 4 - Complications of patients with ABG, according to age group

DISCUSSION

Acute diarrhea remains a very common cause of ED admission, making ABG a condition with relevant epidemiological, economic, and social impact in pediatric age. Acute gastroenteritis usually has a benign and self-limited progression and viral origin. However, the prevalence of bacterial infection is significant.^{3,11,12}

Campylobacter spp. was the main bacteria isolated in the present study, accounting for 72% of positive stool tests, followed by *Salmonella* spp. (22.6%). The higher prevalence of *Campylobacter* spp. compared to other bacteria has been reported in national and international studies.^{8,13,14,16}

Four studies focusing on acute gastroenteritis in pediatric age in Portugal with a similar methodology to the present one have been previously published. Three of these had comparable findings to this study: a multicenter study carried out in the north of Portugal in 2005, a study carried out in Lisbon and Tagus Valley in 2016, and a study carried out in the central region of Portugal in 2014.^{8,9,13-16} In the fourth study, *Salmonella* spp. was the most frequent etiological agent (found in 54% of positive co-cultures), followed by *Campylobacter* spp. (23%).⁹ In another study assessing only hospitalized patients, *Escherichia coli* was the most frequent etiological agent (43%), followed by *Campylobacter* spp. (37%).¹⁵ However, this study had a different methodology from the current one, precluding the comparison of results.¹⁵ Regarding *Campylobacter* species, *C. jejuni* was the most frequently associated with ABG, with an increase in the number of cases diagnosed over the years, in agreement with other studies.^{2,5,8,13}

The percentage of viruses and bacteria coinfection in this study was 7%, a value similar to the one found in the literature.¹³ A higher number of cases was found in children aged between one and five

years, but also a high number of cases in children under one year, in agreement with the recently published national report⁵ and three of the above-mentioned national studies.^{9,13,14} In the study conducted only in patients admitted to the PD,¹⁵ *Campylobacter* spp. was the most frequent pathogen detected in patients aged 12 months and older, and particularly in those over five years. However, this study included a small sample size and hospitalized patients, a population with different clinical characteristics from the one included in the present study. Regarding gender distribution, this study found a predominance of *Campylobacter* spp. in males, also verified in two national studies.^{8,13}

This study has as main limitations its retrospective nature, the use of clinical criteria for performing stool tests, and the scarcity of data available in some clinical records, which hindered the identification of the probable source of infection in some cases and the presence of family cases in others.

Clinical manifestations at presentation were similar between this study and two of the national studies available in the literature.^{9,14} The presentation during the first year of life was similar to other age groups, but seizures were only present in children aged one to five years. According to the literature, aqueous diarrhea is found in about half of cases, which was also observed in this study.^{2,7} The high frequency of cases of diarrhea with blood or mucous in this sample likely represents a data bias related to the fact that stool tests are much more often required in presence of this type of presentation.

Although undeniably relevant from an epidemiological point of view, etiological study is recommended in cases where targeted therapy is indicated or to aid in the differential diagnosis.³ The isolation rate of pathogens in stools in the present study was 32%, similar to that registered in other studies.^{8,9,15}

Importantly, 89 patients (20.2%) were hospitalized in the PD, on

average for 3.2 days, 82 of whom required intravenous hydration. Other studies reported hospitalization rates between 10% and 55%.^{8,9,13,14} As per recommendations, antimicrobial treatment was prescribed in selected cases. Only 11 patients (12.4%) received directed antibiotic therapy (nine azithromycin and two clarithromycin). The very low prescription rate of antibiotics is justified by the fact that treatment of this enteritis is unspecific, and the evolution of bacterial diarrhea is generally self-limited. The choice of medication was mostly empiric, taking into account the most frequently isolated pathogens and their susceptibility. In the group of samples submitted to antibiotic sensitivity test (AST), a pattern of antibiotic resistance similar to the one described in the literature was found, although with a higher rate of quinolone resistance.^{17,18}

At the time of ED discharge, caregivers were educated about warning signs that should be monitored and those requiring prompt medical reassessment. The clinical course was generally favorable, with a low rate of complications and PD admission.

CONCLUSION

ABG in children remains one of the most common causes of hospital admission and a major public health concern in Portugal. *Campylobacter* spp. is currently the most frequent cause of acute bacterial diarrhea in developed countries. An increase in the number of new diagnoses has been reported in recent years for reasons yet to be clarified. Although ABG is mostly a self-limited disease with favorable clinical course, the occurrence of associated complications and/or other forms of more serious and potentially fatal infections should be considered. Stool test enables the etiological identification, which is crucial in cases requiring directed therapy.

The increase in the number of cases diagnosed over the years suggests the need to raise awareness of professionals in primary health care for appropriate hygiene measures in the manipulation and preparation of meals to be conveyed to their patients.

AUTHORSHIP

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REFERENCES

1. Heresi GP, Murphy JR, Cleary TG. *Campylobacter jejuni*. In: Feigin RD, Cherry JD, Demmler-Harrison GJ, Kaplan SL, editors. *Feigin and Cherry's textbook of pediatric infectious diseases*. Philadelphia: Saunders Elsevier; 2009. p. 1612-8.
2. EFSA (European Food Safety Authority), ECDC (European Centre for Disease Prevention and Control). The European Union summary report on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks in 2011. *EFSA J* 2013;11:3129-250.
3. Guarino A, Albano F, Ashkenazi S, Gendrel D, Hoekstra JH, Shamir R, *et al.* European Society for Paediatric Gastroenterology, Hepatology, and Nutrition/European Society for Paediatric Infectious Diseases evidence-based guidelines for the management of acute gastroenteritis in children in Europe. *J Pediatr Gastroenterol Nutr* 2008;46:S81-122.
4. European Centre for Disease Prevention and Control. Annual epidemiological report: Campylobacteriosis. 2016. (Accessed on April 25, 2018). Available in: <https://www.ecdc.europa.eu/en/publications-data/campylobacteriosis-annual-epidemiological-report-2016-2014-data>.
5. Duarte A, Santos A, Benoliel J, Domingues F, Oleastro M. A infecção humana por *Campylobacter* em Portugal: alguns dados epidemiológicos. Instituto Nacional de Saúde Doutor Ricardo Jorge. *Infeções Gastrointestinais. Artigos breves nº7*. 2013.
6. Ketley JM. Pathogenesis of enteric infection by *Campylobacter*. *Microbiology* 1997;143:5-21.
7. Murray PR, Rosenthal KS, Pfaller, MA. *Medical microbiology*. 5th. Philadelphia: Mosby Elsevier; 2005. p.14.
8. Borges AC, Pedrosa C, Santos A, Vitorino M, Costa M, Godinho C. *Campylobacter jejuni*: gastroenterites agudas e infeções extra-intestinais. *Acta Pediatr Port* 2005;36:191-3.
9. Rodrigues F, Calvino J, Alves AF, Lemos L. Diarreia aguda por *Campylobacter* spp. *Acta Pediatr Port* 2006;37:91-4.
10. Ban M Allos. Clinical manifestations, diagnosis, and treatment of *Campylobacter* infection. 2019. (Accessed on August 20, 2018). Available in: <http://www.uptodate.com>.
11. Paiva M, Santos F, Amaral JMV. Gastroenterite aguda. In: Amaral JV, editor. *Tratado de Clínica Pediátrica*. Lisboa: Abbott Lda; 2008. p. 532-6.
12. Bhutta ZA. Acute gastroenteritis in children. In: Kliegman RM, Stanton BF, Schor NF, Geme JW, Behrman RE, editors. *Nelson Textbook of Pediatrics*. Philadelphia: Elsevier Saunders; 2011. p. 1323-38.
13. Peixoto AMM, Brett ACO, Rodrigues FMP. Gastroenterite Aguda Bacteriana num Serviço de Urgência Pediátrico. Faculdade de Medicina da Universidade de Coimbra. 2016.
14. Soares AT, Couto C, Romão P, Melo IS, Braga M, Diogo J, *et al.* Gastroenterite aguda por *Campylobacter* spp: *casuística de uma urgência pediátrica*. *Acta Med Port* 2014;27:556-60.

15. Escobar C, Silva T, Costa B, Oliveira M, Correia P, Ferreira GC, *et al.* Gastroenterite aguda em crianças internadas na área de Lisboa. *Acta Pediatr Port* 2013; 44:148-55.
16. Tam CC, O'Brien SJ, Tompkins DS, Bolton FJ, Berry L, Dodds J, *et al.* Changes in causes of acute gastroenteritis in the United Kingdom over 15 years: microbiologic findings from 2 prospective, population-based studies of infectious intestinal disease. *Clin Infect Dis* 2012;54:1275-86.
17. Lengerh A, Moges F, Unakal C, Anagaw B. Prevalence, associated risk factors and antimicrobial susceptibility pattern of *Campylobacter* species among under five diarrheic children at Gondar University Hospital, Northwest Ethiopia. *BMC Ped* 2013;13:82.
18. Adedayo O, Kirkpatrick BD. *Campylobacter jejuni* infections: update on presentation, diagnosis, and management. *Hosp Physician* 2008;44:9-15.

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